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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/532,834	02/16/2006	Jonathan Michael Blackburn	40418-508N01US	8870

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EXAMINER	
TSAY, MARSHA M	

ART UNIT	PAPER NUMBER
1656	

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04/16/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Advisory Action Before the Filing of an Appeal Brief	**Application No.** 10/532,834	**Applicant(s)** BLACKBURN ET AL.	
	Examiner Marsha M. Tsay	**Art Unit** 1656	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 02 April 2010 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires *6* months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *40-42,44,71,79 and 80*.
   Claim(s) withdrawn from consideration: *45-70 and 72-77*.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
12. ☐ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: _____.

/Maryam Monshipouri/
Primary Examiner, Art Unit 1656

Continuation of 11. does NOT place the application in condition for allowance because: In their remarks after final, Applicants assert (1) Thinakaran does not describe a method in which a lysate comprising a ble fusion protein is contacted with a surface derivatized with a bleomycin family antibiotic, as required by claim 40. In particular, Thinakaran does not describe an in vitro binding assay in which a ble fusion protein binds to an antibiotic. The Examiner asserts that it would be reasonable for the skilled person to translate the use of an in vivo assay (referring to the selection of high expressing cells using antibiotic) to an in vitro assay (referring to the binding assay). However, to the extent Thinakaran teaches in vitro methods they are inapposite to Applicant's claimed invention; the skilled person would have no reason to use the in vitro binding assays described in Thinakaran to assess the binding of ble to an antibiotic because the specific molecules to which ble binds were already known. Moreover, Thinakaran does not direct the skilled person to adapt in vivo binding ofble fusion proteins and antibiotics to an in vitro binding assay because the in vivo binding is used to select for cells expressing high levels of the fusion protein. Teachings that may be relevant for an in vivo assay described in this reference are not applicable to the claimed in vitro methods. Thinakaran's in vivo methods require the cells to be living and multiplying for selection to occur. Applicants' arguments have been fully considered but they are not persuasive.

(1) Response: As noted in the Final office action of December 7, 2009, Thinakaran discloses the use of in vivo cell viability assays (p. 22 [0252]), however, Thinakaran also discloses the use of in vitro assays. The prior art's mere disclosure of more than one alternative does not constitute a teaching away from any of these alternatives because such disclosure does not criticize, discredit, or otherwise discourage the solution claimed.." In re Fulton, 391 F.3d 1195, 1201, 73 USPQ2d 1141, 1146 (Fed. Cir. 2004). In this instance, it would be reasonable for one of ordinary skill to translate the use of an in vivo assay to an in vitro assay because Thinakaran discloses that both types of assays can be used to detect labeled proteins.

Thinakaran discloses a method for screening zeocin resistance in cells expressing a PS1 chimeric polypeptide (p. 21-22 [0248-0252]). A PS1 chimeric polypeptide comprises presenilin fused to YFP (yellow fluorescent protein) and Sh ble (a ble marker protein) (p. 19 [0221]). Therefore, Thinakaran discloses a cell free viability assay that screens for the expression of chimeric polypeptides comprising a ble marker using zeocin. Thinakaran discloses that other proteins, besides presenilins, can be screened for. Further, Thinakaran discloses that cell free assays, i.e. a binding assay, is within the scope of his invention. Thinakaran discloses that the binding assay can be used to assess whether a target molecule can interact with and/or stabilize an unstable protein (p. 9 [0105]). The unstable protein can be in solution, fixed to a support, expressed in a cell, and can be labeled (p. 9 [0105]). Since Thinakaran discloses that the labeled protein can be in solution (which one of ordinary skill would know can be a solution of lysate) and Takagi et al. disclose that the idea of immobilizing antibiotics, i.e. bleomycin, onto the surface of a carrier is known in the art, it would have been obvious to one of ordinary skill at the time the invention was made to modify the method of Thinakaran et al. by immobilizing zeocin onto a surface as suggested by Takagi et al. for screening and/or assessing the binding of a chimeric protein comprising a fluorescent marker and a Sh ble protein marker in an in vitro assay for determining protein binding or stability.

Regarding Applicants' remarks that the skilled person would have no reason to use the in vitro binding assays described in Thinakaran to assess the binding of ble to an antibiotic because the specific molecules to which ble binds were already known, it should be noted that Thinakaran discloses that the binding assay can be used to assess whether a target molecule (i.e. bleomycin) can interact with and/or stabilize an unstable protein (i.e. a chimeric polypeptide comprising a fluorescent marker and a Sh ble protein marker). It is not necessary that the prior art suggest the combination to achieve the same advantage or result discovered by applicant. See, e.g., In re Kahn, 441 F.3d 977, 987, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006). The fact that appellant uses a binding assay in a method for detecting protein expression and folding does not alter the conclusion that its use in a prior art method would have been prima facie obvious from the purpose disclosed in the references, i.e. a method for determining protein stability.

Additional reasons for maintaining the Thinakaran reference are the same as noted in the previous Office action.

The reasons for maintaining the Takagi et al. and Calmels et al. reference are also the same as noted in the previous Office action.